EXPERIMENTAL SYPHILIS IN THE RABBIT.

VI. AFFECTIONS OF BONE, CARTILAGE, TENDONS, AND SYNOVIAL MEMBRANES.

PART I. LESIONS OF THE SKELETAL SYSTEM.

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PLATES 52 TO 60.

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Syphilitic lesions of the skeletal system of the rabbit were first reported by Uhlenhuth and Mulzer (1) in 1910 under the rather indefinite term of "nose tumors." The conditions described by them were produced by intracardial and intravenous injections of massive doses of Treponema pallidum in young rabbits and appear to have been chiefly tumor-like swellings of the nasal mucosa and the soft tissues about the end of the nose. However, periostitis was described in one instance, and subsequent reports (2) contained illustrations of several types of the "nose tumors," which were obviously lesions of the nasal bones and cartilages.

Reasoner (3) also has mentioned the occurrence of a periosteal lesion of the nasal bones and refers to this type of affection as a late manifestation of the infection produced by certain strains of Treponema pallidium. None of these authors indicates the relative incidence of this class of lesions, and these are the only references to lesions of the skeletal system which have come to our notice. Apparently no instance of such a condition has been reported following a local inoculation, unless it be the case referred to by Reasoner.

In our experience, however, localized infections of the skeletal system, including the bones of the feet and legs and face, were quite common, hence it seems that the conditions have passed unrecognized and are, therefore, essentially new additions to the subject of experimental syphilis.

Among our earlier animals, there were 33, or 26 per cent, of those showing manifestations of generalized syphilis, in which lesions of the periosteum, bone, cartilage, tendons, and tendon sheaths were recognized by simple palpation and inspection. With the introduc-
tion of methods intended to increase the incidence and the severity of the generalized infection, as indicated in a previous paper (4), there was a marked increase in this particular group of conditions and the total number of cases available for study was more than doubled. In addition, the use of the radiograph in the diagnosis and study of deep seated lesions has been of considerable advantage.

The majority of the lesions seen were instances of periosteal, perichondrial, or bone involvement; only a few cases were recognized clinically in which the lesions appeared to originate in tendons, tendon sheaths, and like structures, and in a few instances affections of the joints were noted which appeared to be attributable to syphilitic infection. The parts chiefly affected were the facial and cranial bones and cartilages, and the bones, tendons, and joints of the feet, legs, and tail.

All these are lesions of hidden parts and in order to convey some idea of the nature of the processes concerned, it will be necessary to preface the clinical description of this form of experimental syphilis with a brief description of the lesions themselves.

General Character of the Lesions.

Lesions of the skeletal system proper occurred both in the periosteum and in the deeper parts of the bone or cartilage but most of the cases which came under our observation were clearly instances of primary periosteal involvement.

Periosteal Lesions.—These were of two types, the more common one being a nodular, granulomatous condition and the other a process of a more diffuse character. The first was characterized by the formation of small flattened or oval plaques, or of elevated nodules of extreme hardness distributed over the surface of the bones. Some of them spread laterally, forming masses which could barely be detected, while others became more elevated and reached a size of from a few millimeters to more than a centimeter in diameter.

Clinically, these lesions were readily distinguishable from cutaneous affections by the fact that the skin was freely movable over them and they were firmly attached to the underlying bone. When exposed to view, the earlier lesions appeared translucent and of a pale, slightly
yellow color, or presented an opalescent appearance and were surrounded by a faint areola of newly formed vessels. As the lesions developed, they became more dense and changed to a gray or yellowish gray color. Some were highly vascular and showed irregularly distributed areas of congestion and hemorrhage together with foci of necrosis. These conditions may be illustrated in general by Fig. 1, which is a photograph of an autopsy specimen showing the condition present 11 days after the lesions were first noted.

Upon section, some of the lesions were dense and fibrous, while others were more succulent or of a fleshy character. The cut surface of the larger ones frequently presented a mottled appearance due to the presence of irregularly distributed areas of necrosis and hemorrhage. In other cases, the surface was thickly stippled with minute gray or yellow points of necrosis or the entire center of the lesion was necrotic and demarcated from an outer zone of living tissue by the presence of a gray or yellowish gray line (Figs. 2 and 3).

The necrotic portion of the lesion remained firm and elastic, as a rule, but in exceptional instances or in cases of extensive necrosis, the central portion broke down into a softened or a cheesy mass (Fig. 3).

At the beginning, lesions of this type were largely confined to the periosteum, but as the process advanced, they frequently extended to the underlying bone. The changes in the bones themselves were quite variable. In general, they consisted of erosion of the outer table, or of bony caries, and finally led to an osseous overgrowth or the formation of osteophytic nodes. The destructive changes are shown in Figs. 4 and 5.

The first photograph (Fig. 4) shows the condition found at autopsy in an animal with actively progressing lesions of the facial bones. There were three groups of lesions present, the main mass occupying a position over the bridge of the nose while smaller lesions were present on both sides at a slightly higher level.

Upon turning back the flap of periosteum covering the left side of the nose (Fig. 5), the upper lesion appeared as a thickening of the periosteum corresponding with an area of erosion in the bone beneath. Over the bridge of the nose, there was a rather large granulomatous mass, most of which was firmly united with the periosteum. In the position occupied by this mass, a considerable area of the nasal bone had been completely destroyed, exposing the periosteum of the under side of the bone which was also affected. These lesions had been recognizable for only 19 days and yet the degree of destruction was quite marked.
Pathologically, the diffuse periostitis differed from the more circumscribed or nodular form chiefly in the presence of a thin layer of rather soft and friable tissue which covered a wide area of bone. During the earlier stages of the infection, little or no alteration could be detected in the contour of the part, but as the lesions increased, slight thickenings or irregularities could be made out.

On the whole, this type of process appeared to be more destructive than the circumscribed or nodular form; that is, its extension was lateral and inward rather than upward or outward. These lesions also tended to produce a chronic fibrous thickening of the periosteum such as that shown in Figs. 6 and 7. The thickening of the periosteum is here most apparent near the end of the nose where a bulbous enlargement has been produced. This was due in part to periosteal thickening and in part to a thickening of the bone and nasal cartilages (Fig. 7).

With bones such as the nasals, periosteal lesions developed from the under side of the bone as well as from the outer side. This is shown in a low power magnification of a cross-section of the nasal bone reproduced in Fig. 8.

Perichondrial lesions, especially those about the face, presented essentially the same characteristics as those of the periosteum. During periods of active growth, spirochetes could always be demonstrated in these as well as other bone lesions to be described, and were usually present in very large numbers.

Lesions in the Bone and Marrow Cavities.—In addition to primary periosteal involvement with subsequent extension to the bone, a number of lesions were seen which originated within the bone or marrow cavities. This class of infections, including what might be designated as osteitis, osteomyelitis, and epiphysitis or osteochondritis, is still somewhat obscure owing to the difficulty in detecting the lesions at an early stage of their development.

Clinically, little could be told of these affections by ordinary methods of examination until they had reached a fairly advanced stage. Necrosis of such bones as the nasals could then be detected by a crackling or giving of the bone beneath the palpating finger, and as the process extended to the outer surface of the bone, a deformity was produced which in most instances presented the same picture as that
of a primary periostitis. Lesions at the epiphyses of the long bones could also be detected in some instances by the presence of a swelling at the epiphyseal line, but they were difficult to distinguish from periosteal lesions which showed a marked tendency to localize at the same points.

By the use of x-rays, some early lesions were detected and their development was followed, but, as a rule, infection of the deeper parts of the bone was not discovered until the picture had been complicated by necrosis with dissolution of the bone or by pathological fracture. There are, therefore, two groups of conditions to be considered—one including lesions of obvious syphilitic origin and the other affections of a more obscure character.

By radiographs and by pathological examination, lesions were found in both the long and the flat bones. These appeared as focalized processes composed of a pale, translucent, and almost gelatinous material which spread out in the marrow cavities to a greater or less extent and invaded the substance of the bone. A lesion of this type is shown in Fig. 9 which is taken from the so called fifth metatarsal. As may be seen, there were in this case both periosteal and endosteal lesions as well as focal lesions within the bone itself. That the periosteal and endosteal lesions were not parts of the same process could be determined by differences in their histology, but such distinctions could not be made with lesions within the bone.

The internal lesions appeared to arise chiefly from the membrane lining the marrow cavity (endosteum) or in the loose perivascular tissues surrounding the larger vessels. In the long bones, they also showed a predilection for lines of epiphyseal union as shown in Fig. 10. This represents a fully developed lesion which originated in the epiphysis and subsequently spread to other parts of the bone.

Radiographs of the early lesions showed mainly a rarefaction in the bone and a loss of the finer details of structure. These changes may be seen in Fig. 11, which shows two very distinct areas of involvement. One of these is in the shaft of the fifth metatarsal of the right foot (a) and the other at the proximal end of the corresponding bone of the left foot (b). The deformity of the right tarsus and their regularity seen in the calcaneus (c) were the result of an older lesion of a type to be described later.
This class of infections naturally gave rise to pathological alterations in the bone, which were characterized by necrosis with a more or less gradual disintegration of the bone or by increased fragility (when necrosis was more rapid) and the occurrence of pathological fracture or epiphyseal separation.

With these facts in mind, attention may be called to another group of bone lesions whose early stages are very difficult of recognition. These include chiefly cases of necrosis, fracture, and epiphyseal separation of the calcaneus with, occasionally, similar lesions in other bones, and may be illustrated by the affections of the tarsus shown in Figs. 12 to 14.

The history of these affections was much the same in all cases; namely, the sudden development of lameness, with a marked edematous swelling of the entire tarsus together with some tenderness and the presence of a crepitus. The first cases which were noticed were regarded as traumatic injuries and no particular attention was paid to them until it was found that similar conditions occurred as a result of obvious syphilitic infection.

A more careful investigation was then attempted and the nature of the injury to the bone determined by both radiographic and pathological examination. Spirochetes could not be found in fluid aspirated from these cases and the condition was complicated by the reaction incident to the sudden disruption of the bone.

From an examination of serial radiographs of several of these animals, abnormalities of the bones could be made out in some which antedated the occurrence of the lesion in question. In Fig. 15, a peculiar defect is seen in the calcaneus of the right foot. 19 days later, this bone gave way in the middle and anterior portions, permitting the talus to sink downward as shown in Fig. 16, the details of the bony structures being masked at this time by an effusion into the tissues. There was also a dropping of the arch.

A second case is shown in Figs. 17 and 18. The first point to be noted is the dissimilarity of the posterior ends of the calcanei. The left bone shows a narrowing of the neck which extends well below the level of the tuberosity, while on the right, there is even some fullness in this region. This bone shows a band of lighter

1 The demonstration of spirochetes in such cases by animal inoculation would be of no value, since the animals were known to have a generalized infection capable of transmission by blood inoculation.
shadow in the position of the epiphyseal line. 8 days later (Fig. 18) there was an epiphyseal separation, or fracture, which followed this line quite closely. Other examples of a similar character were also seen.

A significant feature of this class of lesions is that among the large number of animals, infected and uninfected, which were handled during the course of this work, with one possible exception, lesions of this type occurred only in animals with obvious syphilitic lesions of other bones (note metatarsals in Figs. 11 and 12). It may be mentioned also that definite periosteal lesions of the anterior end of the calcaneus have been noted, and while no gross destruction of bone was detected in these instances, all the obscure cases of necrosis such as that in Fig. 12 have occurred in exactly the same position as that occupied by the periosteal lesions.

Histologically, however, the extent of bone involvement always proved to be greater than the gross appearance would indicate, and bones which appeared to be very little affected in the gross frequently proved upon histological examination to be honeycombed by the syphilitic process. Further description of these lesions will be found below in the section on the histological changes observed in various types of bone lesions.

Lesions of Tendons and Tendon Sheaths.—There is no record of the occurrence of syphilitic lesions of the tendons or tendon sheaths of the rabbit so far as we are aware, and the number observed by us was comparatively small.

The typical lesion in cases of primary tendon involvement was a circumscribed granulomatous process of essentially the same character as that of the periosteum, and with a few exceptions the lesions were located in the tendo achillis or its sheath. The exceptions noted were small multiple lesions involving the tendons on the dorsum of the carpus and front feet and the dorsum of the hind feet. Some of these were not recognized until the animal came to autopsy, and it is possible that other cases of a similar character might have escaped our notice.

Secondary involvement of tendons and ligaments as a result of direct extension of lesions originating elsewhere was of comparatively frequent occurrence. This was not unusual with periosteal lesions
about the carpus and tarsus and the small bones of the feet, and with cutaneous lesions of the tail and lateral surfaces of the hind feet. Fig. 2 furnishes a good illustration of this type of condition.

**Diffuse Exudative Reactions Associated with Lesions of the Bones.**

In addition to the lesions described, an acute exudative reaction affecting the parts immediately surrounding a focus of bone affection may be referred to briefly. This reaction rarely occurred except with lesions of the tarsus or of the small bones of the feet. In cases of infection of the metatarsals and the phalanges, there was frequently an exudation into the surrounding tissues which was composed chiefly of serum with a few leucocytes and polyblasts. Such reactions occurred most often where there was a considerable degree of bone destruction.

Similar conditions have already been referred to in connection with lesions of the tarsal bones. In addition, there were a few instances in which the reaction occurred where no bone lesion was demonstrable. The inciting factor in these cases is not known, but the subsequent history of the condition, with the development of a diffuse fibrosis and fixation of the affected parts, suggests the possibility of an involvement of synovial membranes of tendon sheaths and joint cavities. Histologically, it has been shown that the *pallidum* infection may become localized in such structures, but whether this takes place by direct extension from other lesions or as an independent focus of infection is as yet undetermined.

**Histology.**

Histologically, the details of the pathological process concerned in syphilitic infections of the bones are too numerous and too complex to be described in the present connection. As a means of orientation, however, it seems well to refer briefly to certain features of the lesions found during active stages of the infection. Three fairly well defined groups of conditions can be recognized: (1) a granulomatous process which is not unlike that of other syphilitic lesions; (2) a condition which is characterized chiefly by absorption or by necrosis and disintegration of bone; and (3) a lesion which combines the processes
of granulomatous proliferation, absorption, and necrosis with osseous overgrowth. This last condition will not be considered at the present time.

The granulomatous lesions usually seen in cases of bone syphilis may arise from any part of the bone and present certain structural peculiarities. In general, they are composed of a matrix of newly formed connective tissue with a network of capillary vessels; there are the usual polyblastic infiltration and a marked tendency on the part of these cells to assume a perivascular arrangement. Polynuclear giant cells are also present and are frequently very numerous, especially where marked bone destruction occurs. The picture presented in these cases is of the type of an active foreign body reaction or may even suggest that of the so called giant cell osteosarcoma.

When the lesion arises from the periosteum, one frequently finds an interesting structural arrangement of the elements which participate in the reaction (Figs. 19 and 20). There are two or three distinct layers which correspond roughly with structural divisions of the periosteum. There is first an outer cellular layer which is composed of loosely arranged connective tissue cells and polyblasts occupying the position of the loose areolar tissue covering the outer surface of the periosteum (Figs. 19 and 20). Then comes a denser layer of fibroblasts which contains numerous focal and perivascular accumulations of round cells and corresponds to the dense fibrous layer of the periosteum. Finally, either as a part of this second stratum or as a distinct layer in itself, there is a zone which corresponds with the osteogenetic layer of the periosteum. At first, this is composed of a row of giant cells (osteoclasts) whose processes dip downward into the bone, and a small amount of newly formed connective tissue infiltrated with polyblastic cells. This is the osteoclastic layer of the lesion and its distinctive elements, the osteoclasts, are derived from the osteoblasts of the periosteum.

The composition of periosteal lesions differs very decidedly in different classes of bones. Thus, in bones which are preformed in membrane, such as the nasal bones, a two layered structure prevails (Fig. 19). This is composed of the loose outer layer and a highly developed third or osteoclastic layer, while the second or fibrous layer is usually absent or but slightly developed. The lesions of the long bones
(cartilage bones), on the other hand, show three layers, the most highly developed of which is the middle or fibrous layer. In addition, the osteoclastic layer is more fibrous and shows relatively few giant cells. These facts are of importance in interpreting the pathological alterations produced in different classes of bones.

The growth of some periosteal lesions is marked by an increase in the thickness of the outer layers, of others by a peripheral extension of all three layers, or by a downward growth of the inner layer. In the first instance, the condition produced is a prominent periosteal nodule, or granuloma, in the second a diffuse periostitis, and in the third marked destruction of the underlying bone. It is in instances of the last group that the osteoclastic layer of the lesion becomes so highly developed; in membrane bones, the greater part of the lesion in such cases presents the picture of the giant cell granuloma, but this is not true of bones which are preformed in cartilage.

Lesions arising within the bone show essentially the same composition as those from the periosteum, except for their structural arrangement, and are, therefore, difficult to distinguish from them. Endosteal affections, on the other hand, are almost devoid of fixed connective tissue elements. They are composed of a loosely arranged stroma which is thickly infiltrated with polyblasts and contains a network of capillary vessels. The lesion is, therefore, more of an infiltrative than of a granulomatous process.

The alterations observed in the bone itself were quite variable. In some instances, the bone presented a practically normal appearance except for the presence of irregularities or a honeycombing of the bone due to gradual absorption, and in some, even small fragments of bone showed a well preserved architecture (Fig. 21). Frequently, however, there were mass necrosis and rapid disintegration of bone extending over wide areas. The picture presented in these cases (Fig. 22) was very striking and consisted of necrosis of bone corpuscles and reduction of the ground substance to a thin and ragged framework of granular or fibrillated material which stained very faintly if at all. The impression created was that of large masses of bone undergoing solution, and various stages in the process could be traced down to the last shadowy framework of fibers and granules (Fig. 22).
Emphasis may be placed upon these processes of bone destruction
on account of the occurrence of similar changes in portions of the
bone where little or no syphilitic reaction of the generally accepted
type could be made out. This was especially noticeable in the lesions
of the calcaneus described above. There were two forms of alteration
to be noted. In one group of cases, the alteration consisted of a
simple bone absorption with reduction in the density and the volume
of the bone; in a second, there were necrosis and disintegration.

The first group developed by widening out of the lacunae and of the
perivascular spaces, which became filled with a loose and rather cellular
connective tissue. The compact portion of long bones such as
metatarsals and phalanges thus tended to become somewhat cancellous in structure, while the cancellous portion of the bone was distinctly reduced in amount. As a result of these changes, there were
a reduction in both the density and the thickness of the bones and a marked enlargement of the marrow cavity. Normally, these bones contain some cellular marrow, but in affections of the type described,
there were not only bone absorption but a conversion of a cellular
(hemopoietic) to a fatty marrow which, in some cases, was complete.

Mass necrosis of portions of the bone which were apparently not
directly involved by the granulomatous lesions needs no further
description than that given above.

The most obvious explanation of these conditions is one based upon
disturbed nutrition. There is little doubt that the primary seat of
injury in all syphilitic processes is the endothelial cell, and while those
in the immediate vicinity of active syphilitic lesions suffer more than
do others, it appears that the effects of the toxic products which are
elaborated may reach every such element of the body. Thus, while
the smaller vessels in the immediate vicinity of a lesion are most
affected, it would seem practically certain that in pronounced cases
of syphilitic infection, the entire capillary mechanism is subjected to
injury the degree of which varies with the individual case.

If this is applied to the bone lesions described, both the absorption
type of phenomenon and the mass necrosis might be accounted for
upon the basis of a reduction in the blood supply due to capillary
injury in the first case and to a more extensive vascular injury in the
second. It would be going too far to assume, however, that other
factors had no part in the production of these lesions, but the reduction of blood supply due to vascular injury appears to be the simplest and most immediate explanation which can be offered.

The fact that rarefaction and necrosis of bone are not necessarily parallel with the size or extent of the granulomatous lesion but may occur even in the absence of any marked granulomatous reaction is of considerable importance, and the obscure cases of necrosis and fracture of the calcaneus described above were largely due to this type of bone lesion.

Histologically, small granulomatous lesions which resemble those of the periosteum or endosteum in all essential respects have been found in the synovial membranes of joint cavities, notably those of the tarsus and the metatarsophalangeal joints. In these cases, there was infection of neighboring parts, and involvement of the joints appeared to have taken place by extension from adjacent foci of infection. While it appears probable, therefore, that primary localization in the joint may occur, this has not as yet been demonstrated.

Gross Alterations in the Bones.

Frequent reference has been made above to various types of bone injury resulting from infection of the periosteum or of the bone itself. Before concluding the description of this group of lesions, it seems well, however, to give a more definite statement as to the gross alterations which are produced.

Nasal Bones and Splints.—The most marked and characteristic lesions were those of the nasal bones and splints. The effects produced may be illustrated by the series of photographs reproduced in Figs. 23 to 30. These photographs were taken from dried skulls and are intended to show alterations produced by focal and diffuse lesions during active stages of the infection as well as the results of repair.

Focal lesions of the nasal bones, as shown in Figs. 23 to 26, may produce anything from the slightest surface erosion or roughening to a complete and sharply circumscribed defect in the bone. All of the group here shown were taken toward the end of the infection and may be regarded, therefore, as representing the maximum of bone destruction produced in each instance. In Fig. 23, there was only a surface erosion, while in the second animal of the series (Figs. 24 and 25) the
necrosis extended much deeper, forming a partial defect in the bone. This defect was easily recognizable during life, and at autopsy it was found that there was little left of the bone except a thin layer of spongy necrotic fragments loosely attached to the underlying membranes. The effect produced in this case might be compared to the saddle-nose deformity of man.

The lesion involving the upper right nasal and the maxillary process of the frontal bone in Fig. 26 shows complete necrosis and removal of the bone, resulting in the formation of a small but very sharply circumscribed defect. It should be stated that the clean-cut appearance presented by this lesion was probably due to the fact that it was of internal rather than external origin. There was a very slight external growth in this case, and when this first appeared, necrosis of the bone had already taken place.

The conditions represented in Figs. 27 and 28 differ from those preceding only in that they represent processes of a more diffuse character, which, as has been explained, are usually more destructive in their effects.

Figs. 29 and 30 represent processes of repair. The lesion in Fig. 29 was of the same type as that in Figs. 27 and 28, but led to complete necrosis of a large part of both nasal bones. The condition here shown is the regeneration effected during a period of about 7 weeks. The bones were considerably thickened throughout; in the upper portion, regeneration was very imperfect, and while the bone towards the end of the nose was of a decidedly spongy character, it was much more nearly normal than that above and the probability is that in time the entire area would have assumed this appearance.

This case illustrates a remarkable tendency on the part of the rabbit to an obliteration of the marks of syphilitic lesions in the bones. Small erosions and defects of the nasal bones are usually repaired so as to leave little if any evidence of the previous injury, and the permanent alterations produced by the most destructive lesions are much less than one might expect. This evidence usually consists of a thickened and adherent periosteum, slight irregularities in the bone, surface roughening and thickening of the bone (cf. Figs. 6 and 7), and the presence of slight depressions or bony prominences. The last conditions are occasionally fairly well marked, as indicated by the node on the nasal splint in Fig. 30.

Anomalous Conditions of the Parietals and Occipitals.—Before leaving this phase of bone syphilis, attention may be called to the condition of the parietal and occipital bones shown in Fig. 31. The cause of this condition is not known, but, as may be seen, there is a decided thickening of the bones which are very porous or spongy in character.
Various degrees of this condition have been observed at autopsy in a number of animals. Most of them were instances of long standing syphilitic infection; some animals were in excellent physical condition, while others showed obvious signs of malnutrition for which no cause could be found. In some, the bones contained an abundant red marrow; in others, the marrow was more fatty in character.

It is, of course, well known that similar changes in these bones may be produced through the development of an anemia, and there is at present no reason to regard the processes here shown as the result of a local infection. The circumstances suggest, however, that they may be produced in response to a systemic condition resulting from the syphilitic infection.

Ulna, Radius, and Tibiofibular.—Many of the long bones such as the ulna, the radius, and the tibiofibular show little alteration in appearance at any stage of the infection. Usually there was no more than a slight roughening of the surface of the bone with either an increase or a decrease in thickness. These areas also showed a honeycombing of the bone, but the apparent alteration was always less than that shown by microscopic examination.

The tendency was also towards a rapid restoration to normal, and bones examined a few months after the lesion had resolved showed little if any abnormality.

Metatarsals and Phalanges.—Gross changes in the metatarsals and the phalanges were more marked. During the active stages of the infection, there were usually surface erosion, necrosis, and disintegration, epiphyseal separation, or fracture. Less often, osseous overgrowth or the laying down of considerable masses of soft, spongy bone occurred, while the lesion was still actively progressing (Fig. 10).

As the infection subsided and the injury to the bone was repaired, various abnormalities were observed. These consisted of changes in the form of the bone, surface roughening, and honeycombing, together with irregular reductions or increases in thickness such as were illustrated for the nasal bones. Many of these changes appeared to be of a semipermanent character. The abnormality diminished with time, but in a few animals which were held for observation, marks of the previous injury were still recognizable several months after the infection had subsided.
Tarsus.—Deformities of the tarsus following necrosis, fracture, or epiphyseal separation of the calcaneus were always marked. These conditions invariably led to excessive bone formation. Necrosis and disintegration of the calcaneus were followed by the formation of an irregular granular mass of bone such as that shown in Fig. 32. The union of a fracture or of an epiphyseal separation, on the other hand, was accomplished by the laying down of an excessive amount of callus and the formation of a large mass of spongy bone (Fig. 33). These conditions were also of a more or less permanent character. The absorption of callus and the reestablishment of compact bone took place slowly—more slowly than after ordinary trauma.

SUMMARY.

From a study of a series of rabbits inoculated with two old strains of Treponema pallidum, it was found that localized infection of bones and tendons was of frequent occurrence and led to the formation of a variety of lesions.

The bones usually involved were those of the face and the feet and legs. Most often the lesions arose from the periosteum but developed also within the bone or marrow cavities and at lines of epiphyseal union.

Grossly, the periosteal lesions were of two types—one being a circumscribed, indurated, and nodular mass and the other a process of a more diffuse character. Histologically, the lesions presented the typical appearance of syphilitic granulomata composed of more or less distinct layers which corresponded roughly with structural divisions of the periosteum. The composition of lesions of membrane and of cartilage bones differed somewhat in this respect, especially in the development of an osteoclastic layer. Invasion of the bone with absorption and necrosis were constant features of periosteal affections and were most marked in the case of the facial bones and the small bones of the feet.

Lesions in the bone and marrow cavities were detected chiefly by radiographs or by the occurrence of bone destruction in the absence of periosteal involvement. They were characterized by a loss of structural detail in the bone, rarefaction, increased fragility, necrosis,
pathological fracture, and epiphyseal separation associated with more or less granulomatous reaction. Histologically, the bone lesions presented essentially the same picture as those of the periosteum, while the lesions which arose from the marrow cavities were composed chiefly of polyblastic infiltrations. In this group of affections, the most important were those which developed at the epiphyses.

The destructive effects produced by all classes of lesions varied from a slight surface erosion or rarefication to extensive necrosis resulting in the formation of bony defects or in disintegration or fracture of the bone. These conditions differed very decidedly with the particular bones involved.

Of especial importance in this connection was the occurrence of a peculiar form of mass necrosis which at times resulted in the destruction of considerable areas of bone even in parts where the granulomatous type of lesion was comparatively slight. The most characteristic injuries were the saddle-nose deformities and the epiphyseal separation in the small bones of the tarsus and hind feet.

The marks of permanent injury were, on the whole, comparatively slight, but they also differed both with the degree of the original injury and with the bone affected.

Granulomatous lesions of tendons or tendon sheaths were occasionally seen, and in a few instances, lesions of synovial cavities were demonstrated microscopically.

BIBLIOGRAPHY.

EXPLANATION OF PLATES.

The photographs and radiographs represent the objects at their natural size. None of the illustrations has been retouched. Statements of time, unless otherwise indicated, are estimated from the date of inoculation.

PLATE 52.

FIGS. 1 to 7. Nodular and diffuse periostitis.

Fig. 1. 74 days. Typical periosteal granulomata of the nasal bones, growth tending to be upward rather than inward.

Fig. 2. 123 days. Periosteal granuloma on the shaft of the fifth metatarsal and involving the tendons of the dorsum of the foot. The cut surface shows irregular miliary areas of necrosis.

Fig. 3. 137 days. Periosteal granulomata of the tibiofibular, the fifth metatarsal, and the phalanges. The lesion of the tibiofibular shows a central area of necrosis with softening and a mottling due to congestion and hemorrhage.

Fig. 4. 84 days. Multiple periosteal lesions of the nasal bones.

Fig. 5. The same specimen with the periosteum dissected back. The lesion on the upper part of the nasal bone is of slight extent and shows only a surface erosion of the bone; that over the bridge of the nose is composed chiefly of an osteoclastic growth, and there are complete necrosis and absorption of the bone in this area.

Fig. 6. 2 years and 5 months. Chronic fibrous periostitis of the nasal bones of a diffuse type. The main lesions appear as bulbous masses at the end of the nose.

Fig. 7. The same preparation with the periosteum removed from the left side. There is an irregular thickening of the bone which is most evident in the lower third, and the periosteum was firmly adherent at many points. Note also the irregularity of the end of the nasal bone.

PLATE 53.

Fig. 8 and 9. Photomicrographs of periosteal and endosteal granulomata.

Fig. 8. 48 days. Cross-section of nasal bone showing periosteal and perichondrial lesion arising from the inner side of the bone and working its way outward. The external coverings of the bone are normal. × 95.

Fig. 9. 89 days. Proximal end of the fifth metatarsal. The photograph shows a combination of lesions, the chief one being a granulomatous nodule in the marrow cavity; there is a distinct widening of this part of the cavity. Lesions are also seen in the bone and on both periosteal surfaces. × 30.

PLATE 54.

Fig. 10. 89 days. An epiphyseal lesion of the distal end of the fifth metatarsal. There has been a separation of the epiphysis which apparently took place in the directions indicated by the arrows. At the time represented in the photograph,
this lesion was in progress of repair but there was an active syphilitic granuloma in the epiphysis. A periostitis is also seen to be present and there is an extension of the infection to the synovial membranes lining the joint cavity. × 30.

Plate 55.

Figs. 11 to 14. Radiographs of lesions developing within the bones.
Fig. 11. 119 days. The rarefaction seen at a and b was due to osteitis of the shaft and proximal end of the metatarsals. The deformity of the tarsus at c was due to necrosis of the calcaneus.
Fig. 12. 163 days. Necrosis of the anterior end of the right calcaneus (marked by arrow). There were lesions also at the proximal ends of both lateral metatarsals (marked by arrows).
Fig. 13. 77 days. Pathological fracture of the middle of the calcaneus with effusion into the tissues.
Fig. 14. 73 days. Epiphyseal separation of the right calcaneus. The left calcaneus also shows some degree of abnormality which is indicated chiefly by the thickening of the upper surface of the bone toward its posterior extremity. Normally the shadow of this portion of the bone forms a straight line (cf. other radiographs).

Plate 56.

Figs. 15 to 18. Radiographs showing lesions of the bone.
Figs. 15 and 16. Successive stages in the development of a lesion of the right calcaneus. Fig. 15 (85 days) shows a peculiar defect in the lower portion of the calcaneus which is marked by an arrow. The left calcaneus is normal. Fig. 16, which was taken 19 days later, shows an outspoken deformity of the right calcaneus. This was due in part to a dropping of the arch from involvement of the ligaments and in part to necrosis of the calcaneus, the talus becoming embedded in its substance. Note the relative position of the talus in Figs. 15 and 16.
Figs. 17 and 18. Stages in the development of an epiphyseal separation. In Fig. 17 (77 days) there is a broad band of rarefaction at the epiphyseal line of the right calcaneus (marked by arrow) and a suggestion of a separation is seen at the top of this line. The posterior end of the left calcaneus also shows a narrowing of the neck which is abnormal. Fig. 18, taken 8 days later, shows a separation of the epiphysis of the right calcaneus which followed the line indicated in Fig. 17.

Plate 57.

Figs. 19 and 20. Photomicrographs showing characteristic periosteal lesions of membrane and cartilage bone.
Fig. 19. 60 days. Periostitis of the nasal bone showing an outer cellular layer and an inner osteoclastic layer. The cellular layer is composed chiefly of fibroblasts with a moderate degree of polyblastic infiltration. It is also quite vascular. The osteoclastic layer is composed of fibroblasts and polyblasts together with a large number of osteoclastic cells. × 95.
FIG. 20. 77 days. Periostitis of the metatarsal. The lesion shows three distinct layers which present much the same general appearance. The two outer layers show a considerable degree of polyblastic infiltration; they are more vascular than the inner layer and the vessels show well marked endarteritis. The osteoclastic layer is but slightly developed; it is largely fibrous in character and contains very few osteoclasts. × 95.

PLATE 58.

FIGS. 21 and 22. Photomicrographs, taken from the nasal bone, showing different types of bone destruction.

FIG. 21. 60 days. Necrosis and absorption of bone accomplished chiefly by surface action. Note the wave lines in the bone, the preservation of architecture, and the survival of bone corpuscles. × 135.

FIG. 22. 100 days. Mass necrosis with rapid disintegration of bone—a type of lesion frequently observed in cases of marked bone destruction as it occurs in an acutely progressive process. × 135.

PLATE 59.

FIGS. 23 to 26. Photographs of dried preparations showing the maximum bone injury produced by various types of lesions.

FIG. 23. 121 days. Surface erosion of the nasal bones produced by a large periosteal granuloma, the growth of which was mostly in the outer layers.

FIG. 24. 118 days. Necrosis of the nasal bones with the production of saddle-nose deformity due to an invasive periosteal lesion.

FIG. 25. The same specimen viewed from the side.

FIG. 26. 124 days. A defect of the right nasal bone produced by a lesion arising from the inner side of the bone. There was only a suggestion of periosteal thickening in this area.

PLATE 60.

FIGS. 27 to 33. Bone lesions and the deformities produced in the process of repair.

FIG. 27. 123 days. A widespread necrosis of the nasal bones resulting from a diffuse periostitis which produced only a slight palpable thickening over the surface of the bone.

FIG. 28. 137 days. Similar lesion viewed from the side. Note especially the destruction of the margin of the bone, the involvement of the lateral splints, and extension of the lesion to the premaxilla.

FIG. 29. 121 days. An imperfect regeneration of the nasal bones following almost complete necrosis of the areas involved. In the upper portion of the right nasal, the bone is very irregular, while below it is comparatively smooth but considerably thickened, and a defect is still present in this part of the bone.
FIG. 30. 130 days. An osteophytic node at the point of union of the frontal process of the premaxilla and the maxillary process of the frontal bone (nasal splints), illustrating a tendency of syphilitic lesions to become localized at points of bony union.

FIG. 31. 342 days. A thickened spongy condition of the parietal and occipital bones occurring late in the course of a generalized infection. The exact cause of the condition is not known.

FIG. 32. 126 days. A deformity of the tarsus resulting from necrosis of the calcaneus. This bone is considerably thickened and extremely irregular.

FIG. 33. 126 days. A deformity produced by an epiphyseal separation of the calcaneus. The original lesion healed with the formation of a large mass of callus about the posterior end of the calcaneus and the separated epiphysis.
(Brown, Pearce, and Witherbee: Experimental syphilis in the rabbit. VI.)
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